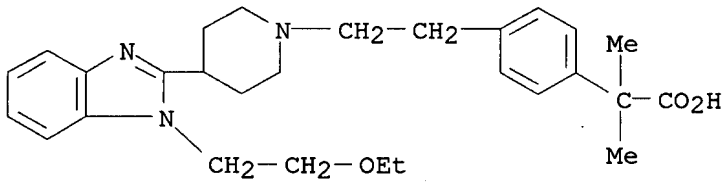
L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 202189-78-4 REGISTRY
ED Entered STN: 05 Mar 1998
CN Benzeneacetic acid, 4-[2-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperidinyl]ethyl]-α,α-dimethyl- (CA INDEX NAME)
OTHER NAMES:
CN Bilastine
MF C28 H37 N3 O3
SR CA
LC STN Files: ADISINSIGHT, ANABSTR, BIOSIS, CA, CAPLUS, CBNB, CHEMCATS, IMSDRUGNEWS, IMSRESEARCH, PHAR, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> FILE REG

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	25.20	54.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.78

FILE 'REGISTRY' ENTERED AT 08:24:41 ON 21 NOV 2007
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 20 NOV 2007 HIGHEST RN 955158-15-3
DICTIONARY FILE UPDATES: 20 NOV 2007 HIGHEST RN 955158-15-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> STR 202189-78-4

:END

L8 STRUCTURE CREATED

=> S L8 FAM FUL

FULL SEARCH INITIATED 08:24:45 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 15 TO ITERATE

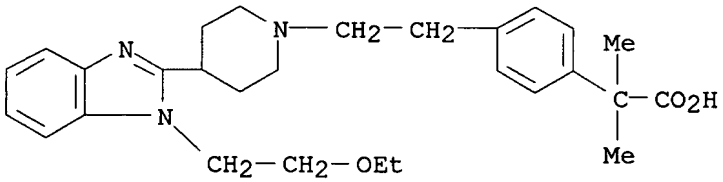
100.0% PROCESSED 15 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

L9 1 SEA FAM FUL L8

=>

=> D SCAN

L9 1 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN Benzeneacetic acid, 4-[2-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperidinyl]ethyl]-α,α-dimethyl-
MF C28 H37 N3 O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	67.70	121.98

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.78

FILE 'CAPLUS' ENTERED AT 08:25:01 ON 21 NOV 2007
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FILE COVERS 1907 - 21 Nov 2007 VOL 147 ISS 22
FILE LAST UPDATED: 20 Nov 2007 (20071120/ED)

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http://www.cas.org/infopolicy.html

=> s l7
L10 6 L7

=> d bib abs hitstr 1-6

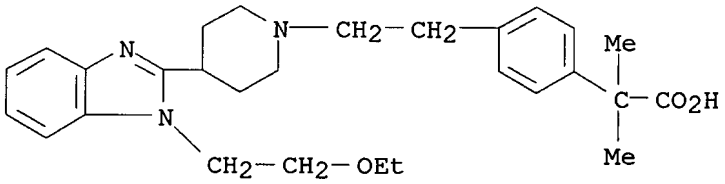
L10 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:407984 CAPLUS
DN 146:408406
TI Pharmaceutical formulations of cyclodextrins and antifungal azole compounds
IN Buchanan, Charles Michael; Buchanan, Norma Lindsey; Lambert, Juanelle Little
PA USA
SO U.S. Pat. Appl. Publ., 22pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007082870	A1	20070412	US 2006-545516	20061011
WO 2007047253	A2	20070426	WO 2006-US39512	20061011

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

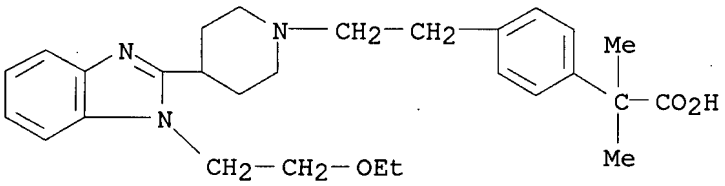
PRAI US 2005-724792P P 20051011
AB This invention relates to methods of increasing the aqueous solubility of an antifungal azole using hydroxybutenyl cyclodextrins. This invention also relates to method of increasing the bioavailability of an antifungal azole compds. administered to subjects. Iraconazole-hydroxybutenyl-γ-cyclodextrin complex was prepared and its bioavailability was studied in rats. The bioavailability of the complex was 52% as compared with 32% for oral solns.
IT 202189-78-4, Bilastine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulations of cyclodextrins and antifungal azole compds.)

RN 202189-78-4 CAPLUS
CN Benzeneacetic acid, 4-[2-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperidinyl]ethyl]-α,α-dimethyl- (CA INDEX NAME)



L10 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:868794 CAPLUS
DN 146:220739
TI In vivo pharmacological characterisation of bilastine, a potent and selective histamine H1 receptor antagonist
AU Corcostegui, Reyes; Labeaga, Luis; Innerarity, Ana; Berisa, Agustin; Orjales, Aurelio
CS Department of Research, FAES FARMA, S.A., Leioa, Spain
SO Drugs in R&D (2006), 7(4), 219-231
CODEN: DRDDFD; ISSN: 1174-5886
PB Adis International Ltd.
DT Journal
LA English
AB Objective: We set out to establish the in vivo histamine H1 receptor antagonistic (antihistaminic) and antiallergic properties of bilastine. Methods: In vivo antihistaminic activity expts. consisted of measurement of inhibition of increase in capillary permeability and reduction in microvascular extravasation and bronchospasm in rats and guinea pigs induced by histamine and other inflammatory mediators; and protection against lethality induced by histamine and other inflammatory mediators in rats. In vivo antiallergic activity expts. consisted of measurement of passive and active cutaneous anaphylactic reactions as well as type III and type IV allergic reactions in sensitized rodents. Results: In the in vivo antihistaminic activity expts., bilastine was shown to have a pos. effect, similar to that of cetirizine and more potent than that of fexofenadine. The results of the in vivo antiallergic activity expts. showed that the properties of bilastine in this setting are similar to those observed for cetirizine and superior to fexofenadine in the model of passive cutaneous anaphylactic reaction. When active cutaneous anaphylactic reaction expts. were conducted, bilastine showed significant activity, less potent than that observed with cetirizine but superior to that of fexofenadine. Evaluation of the type III allergic reaction showed that of the antihistamines only bilastine was able to inhibit edema in sensitized mice, although its effect in this respect was much less potent than that observed with dexamethasone. In terms of the type IV allergic reaction, neither bilastine, cetirizine nor fexofenadine significantly modified the effect caused by oxazolone. Conclusions: The results of our in vivo preclin. studies corroborate those obtained from previously conducted in vitro expts. of bilastine, and provide evidence that bilastine possesses antihistaminic as well as antiallergic properties, with similar potency to cetirizine and superior potency to fexofenadine.
IT 202189-78-4, Bilastine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bilastine showed antihistaminic and antiallergic activities in rat and guinea pig)
RN 202189-78-4 CAPLUS
CN Benzeneacetic acid, 4-[2-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-

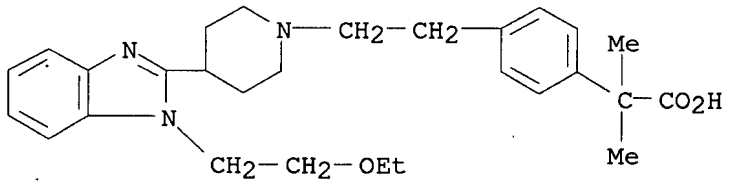
piperidinyl]ethyl]-α,α-dimethyl- (CA INDEX NAME)



RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:28162 CAPLUS
DN 144:425455
TI Preclinical pharmacology of bilastine, a new selective histamine H1 receptor antagonist. Receptor selectivity and in vitro antihistaminic activity
AU Corcostegui, Reyes; Labeaga, Luis; Innerarity, Ana; Berisa, Agustin; Orjales, Aurelio
CS Department of Research, FAES FARMA, Leioa, Spain
SO Drugs in R&D (2005), 6(6), 371-384
CODEN: DRDDFD; ISSN: 1174-5886
PB Adis International Ltd.
DT Journal
LA English
AB Objective: This study aimed to establish the receptor selectivity and antihistaminic activity of bilastine, a new selective antihistamine receptor antagonist. Design and methods: In vitro expts. were conducted using a receptor binding screening panel and guinea-pig and rat tissues. Antihistaminic activity was determined using H1 receptor binding studies and in vitro H1 antagonism studies conducted in guinea-pig tissues and human cell lines. Receptor selectivity was established using a receptor binding screening panel and a receptor antagonism screening conducted in guinea-pig, rat and rabbit tissues. Inhibition of inflammatory mediators was determined through the Schultz-Dale reaction in sensitized guinea-pig ileum. Results: Bilastine binds to histamine H1-receptors as indicated by its displacement of [3H]-pyrilamine from H1-receptors expressed in guinea-pig cerebellum and human embryonic kidney (HEK) cell lines. The studies conducted on guinea-pig smooth muscle demonstrated the capability of bilastine to antagonize H1-receptors. Bilastine is selective for histamine H1-receptors as shown in receptor-binding screening conducted to determine the binding capacity of bilastine to 30 different receptors. The specificity of its H1-receptor antagonistic activity was also demonstrated in a series of in vitro expts. conducted on guinea-pig and rat tissues. The results of these studies confirmed the lack of significant antagonism against serotonin, bradykinin, leukotriene D4, calcium, muscarinic M3-receptors, α1-adrenoceptors, β2-adrenoceptors, and H2- and H3-receptors. The results of the in vitro Schultz-Dale reaction demonstrated that bilastine also has anti-inflammatory activity. Conclusions: These preclin. studies provide evidence that bilastine has H1-antihistamine activity, with high specificity for H1-receptors, and poor or no affinity for other receptors. Bilastine has also been shown to have anti-inflammatory properties.
IT 202189-78-4, Bilastine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bilastine selectively showed antagonistic effect on histamine H1 receptors in guinea-pig cerebellum, HEK cell line and exhibited anti-anaphylactic activity than cetirizine, fexofenadine on sensitized

guinea-pig ileum)
RN 202189-78-4 CAPLUS
CN Benzeneacetic acid, 4-[2-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperidinyl]ethyl]-α,α-dimethyl- (CA INDEX NAME)



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:855922 CAPLUS
DN 139:350736
TI Preparation of a new polymorph of 4-[2-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperidinyl]ethyl]-α,α-dimethylbenzeneacetic acid (bilastine) as an antihistaminic and antiallergic agent
IN Orjales Venero, Aurelio; Bordell Martin, Maravillas; Canal Mori, Gonzalo; Blanco Fuente, Haydee; Lucero de Pablo, Maria Luisa; Rubio Royo, Victor; Mosquera Pestana, Ramon
PA Faes Farma, S.A., Spain
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA Spanish
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003089425	A1	20031030	WO 2002-ES194	20020419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2484460	A1	20031030	CA 2002-2484460	20020419
AU 2002255017	A1	20031103	AU 2002-255017	20020419
BR 2002015703	A	20050201	BR 2002-15703	20020419
EP 1505066	A1	20050209	EP 2002-724323	20020419
EP 1505066	B1	20061206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1628112	A	20050615	CN 2002-828987	20020419
HU 2005000241	A2	20050628	HU 2005-241	20020419
JP 2005529120	T	20050929	JP 2003-586146	20020419
NZ 536551	A	20060831	NZ 2002-536551	20020419
RU 2288917	C2	20061210	RU 2004-133813	20020419
AT 347550	T	20061215	AT 2002-724323	20020419
ES 2278018	T3	20070801	ES 2002-2724323	20020419
MX 2004PA10313	A	20050608	MX 2004-PA10313	20041019
IN 2004KN01735	A	20050902	IN 2004-KN1735	20041116

	NO 2004004999	A	20050114	NO 2004-4999	20041117
	ZA 2004009217	A	20060222	ZA 2004-9217	20041117
	BG 108941	A	20051230	BG 2004-108941	20041118
	US 2005203141	A1	20050915	US 2005-511822	20050323
	HK 1072772	A1	20070309	HK 2005-106418	20050727
PRAI	EP 2002-724323	A	20020419		
	WO 2002-ES194	W	20020419		

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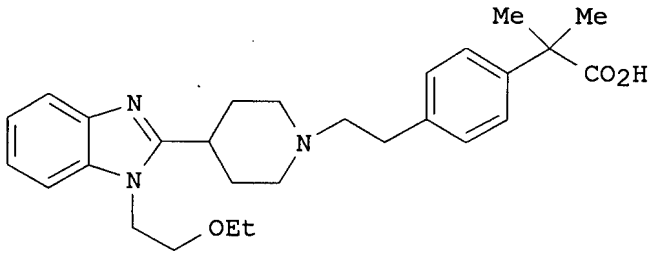


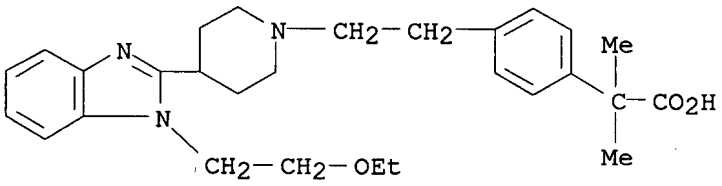
I

AB The invention is directed to the preparation of a new polymorph of 4-[2-[4-[1-(2-ethoxyethyl)-1H-benzimidazole-2-il]-1-piperidinyl]ethyl]-α,α-dimethylbenzeneacetic (bilastine) I, its pharmaceutical formulations and its use for treatment of allergic reactions and pathol. processes mediated by histamine in mammals such as humans. Specifically, the polymorph of I, melting at 200.3° (II), was prepared, in high yield, by recrystn. of bilastine (prepared according to US Patent 5,877,187) or its unstable polymorphs from short chain alcs. (i-PrOH and BuOH), acetone or their mixts. and was characterized by X-ray crystallog. and IR (in KBr). II and its pharmaceutical compns. are stable at room temperature and are useful as antihistaminic and antiallergic agents (no data).

IT 202189-78-4P, Bilastine
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of a new polymorph of bilastine as antihistaminic and antiallergic agent by recrystn. from short chain alcs.)

RN 202189-78-4 CAPLUS

CN Benzeneacetic acid, 4-[2-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperidinyl]ethyl]-α,α-dimethyl- (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:538628 CAPLUS

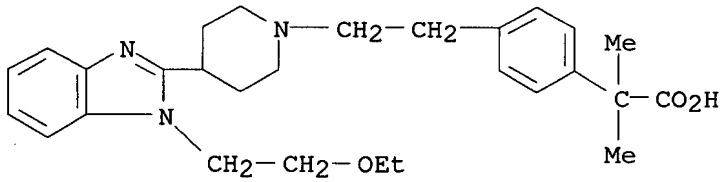
DN 135:366280

TI Matrix solid-phase dispersion technique for the determination of a new antiallergic drug, bilastine, in rat faeces

AU Berrueta, L. A.; Fernandez-Armentia, M.; Bakkali, A.; Gonzalo, A.; Lucero, M. L.; Orjales, A.

CS Faculty of Sciences, Analytical Chemistry Department, University of the

Basque Country, Bilbao, 48080, Spain
SO Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 760(1), 185-190
CODEN: JCBBEP; ISSN: 0378-4347
PB Elsevier Science B.V.
DT Journal
LA English
AB A matrix solid-phase dispersion (MSPD) procedure for the isolation and HPLC determination of a new antiallergic agent, bilastine, in rat feces is presented. The effect on recovery of empirical variables such as nature, pH and volume of the washing and elution liqs. and nature of the adsorbent has been tested. The best recoveries were attained using an octadecylsilyl sorbent, 10 mL of a 0.1 M NaHCO3-Na2CO3 aqueous buffer of pH 10.0 as washing solvent and 10 mL of methanol as elution solvent. The exts. were evaporated to dryness and reconstituted in mobile phase before their injection into a HPLC system, equipped with a Discovery RP-amide C16 column and a fluorescence detector. The method allows one to reach recoveries of 95.0% within the concentration range 0.05-10 μg/g, with within-day repeatabilities of less than 5% and between-day repeatabilities of less than 9% within this range. This method has been successfully applied to the excretion studies of bilastine in the rat.
IT 202189-78-4, Bilastine
RL: ANT (Analyte); ANST (Analytical study)
(matrix solid-phase dispersion technique for determination of new antiallergic
drug, bilastine, in rat feces)
RN 202189-78-4 CAPLUS
CN Benzeneacetic acid, 4-[2-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperidinyl]ethyl]-α,α-dimethyl- (CA INDEX NAME)



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

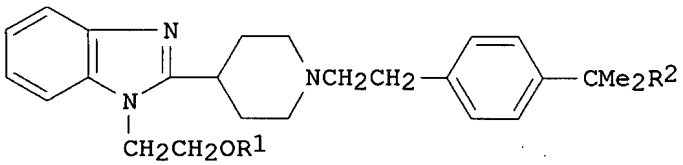
L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:126216 CAPLUS
DN 128:140702
TI Benzimidazole derivatives with antihistaminic activity
IN Orjales, Aurelio; Rubio, Victor; Bordell, Maravillas
PA Fabrica Espanola de Productos Quimicos y Farmaceuticos, S.A. (Faes), Spain
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 818454	A1	19980114	EP 1997-500099	19970603
	EP 818454	B1	20040414		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
	ES 2124167	A1	19990116	ES 1996-1236	19960604
	ES 2124167	B1	19990916		
	CA 2206754	A1	19971204	CA 1997-2206754	19970603

	CA 2206754	C	20070123		
	NO 9702525	A	19971205	NO 1997-2525	19970603
	NO 313195	B1	20020826		
	AU 9724672	A	19971211	AU 1997-24672	19970603
	AU 725700	B2	20001019		
	ZA 9704893	A	19971230	ZA 1997-4893	19970603
	HR 970307	B1	20020228	HR 1997-307	19970603
	RU 2182150	C2	20020510	RU 1997-108980	19970603
	AT 264317	T	20040415	AT 1997-500099	19970603
	PT 818454	T	20040831	PT 1997-500099	19970603
	JP 10059961	A	19980303	JP 1997-162010	19970604
	CN 1176964	A	19980325	CN 1997-114905	19970604
	CN 1105716	B	20030416		
	US 5877187	A	19990302	US 1997-868743	19970604
	HU 9700997	A1	19990928	HU 1997-997	19970604
	IN 186319	A1	20010804	IN 1997-DE1498	19970604
	CZ 289278	B6	20011212	CZ 1997-1723	19970604
	BR 9703276	A	20040817	BR 1997-3276	19970604
	PL 188908	B1	20050531	PL 1997-320358	19970604
	MX 9704127	A	20050725	MX 1997-4127	19970604
	TW 438794	B	20010607	TW 1997-86110371	19970722
	IN 2000DE01067	A	20060331	IN 2000-DE1067	20001128
	IN 2000DE01068	A	20060414	IN 2000-DE1068	20001128
	IN 2000DE01069	A	20060714	IN 2000-DE1069	20001128
	IN 2000DE01071	A	20070309	IN 2000-DE1071	20001128
PRAI	ES 1996-1236	A	19960604		
	IN 1997-DE1498	A3	19970604		

OS MARPAT 128:140702

GI



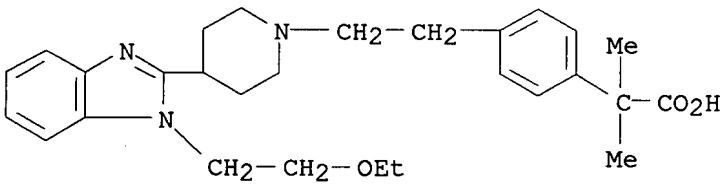
I

AB New benzimidazole derivs. I [R1 = H or a short chain hydrocarbon group such as Me, Et, iso-Pr, cyclopropyl, vinyl, etc.; R2 = CH2OH, CO2H, CO2R3, 4,4-dimethyl-2-oxazolinyl; R3 = short chain alkyl, such as Me, Et], which have high H1 antihistaminic and antiallergic activity and are devoid of effects on the central nervous and cardiovascular systems, were prepared Thus, 2-(4-(1-(4,4-dimethyl-2-oxazolin-2-yl)-1-methylethyl)phenyl)ethyl p-toluenesulfonate was treated with 2-(4-piperidinyl)-1H-benzimidazole to give I [R1 = Et, R2 = 4,4-dimethyl-2-oxazolin-2-yl] which was hydrolyzed to I [R1 = Et, R2 = CO2H].

IT 202189-78-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of antihistaminic and antiallergic benzimidazolylpiperidinylethylphenylacetic acid derivs.)

RN 202189-78-4 CAPLUS

CN Benzeneacetic acid, 4-[2-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperidinyl]ethyl]-α,α-dimethyl- (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT